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Applicant Aarhus Universitet et al.

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Amended Claims

1. A method for estimating the skin cancer, lung cancer, breast cancer and colon

5   cancer risk of an individual comprising

-   assessing in the genetic material of a sample from said individual a sequence
    polymorphism

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-   in a region corresponding to SEQ ID NO: 2, or a part thereof, or
-   in a region complementary to SEQ ID NO: 2, or a part thereof, or
-   in a transcription product from a sequence in a region corresponding to SEQ
    ID NO: 2, or a part thereof, or
15
-   or translation product from a sequence in a region corresponding to SEQ ID
    NO: 2, or a part thereof,
-   obtaining a sequence polymorphism response,

-   estimating the skin cancer, lung cancer, breast cancer and colon cancer risk of
20   said individual based on the sequence polymorphism response.

2. The method according to claim 1, wherein a sequence polymorphism is as-
    sessed

25   - in a region corresponding to SEQ ID NO: 1, or a part thereof, or
        - in a region complementary to SEQ ID NO: 1, or a part thereof, or
        - in a transcription product from a sequence in a region corresponding to SEQ ID
        NO: 1, or a part thereof, or
        - or translation product from a sequence in a region corresponding to SEQ ID
30   NO: 1, or a part thereof.

3. The method according to claim 1, wherein the cell sample is a blood sample, a
    tissue sample, a sample of secretion, semen, ovum, a washing of a body sur-
    face, such as a buccal swap, a clipping of a body surface, including hairs and
35   nails.

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4. The method according to any of the preceding claims, wherein the cell is selected from white blood cells and tumor tissue.

5. The method according to any of the preceding claims, wherein the sequence polymorphism comprises at least one mutation base change.

6. The method according to any of the preceding claims, wherein the sequence polymorphism comprises at least two base changes.

7. The method according to any of the preceding claims, wherein the sequence polymorphism comprises at least one single nucleotide polymorphism.

8. The method according to any of the preceding claims, wherein the sequence polymorphism comprises at least two single nucleotide polymorphisms.

9. The method according to any of the preceding claims, wherein the sequence polymorphism comprises at least one tandem repeat polymorphism.

10. The method according to any of the preceding claims, wherein the sequence polymorphism comprises at least two tandem repeat polymorphisms.

11. The method according to any of the preceding claims, wherein the assessment is conducted by means of at least one nucleic acid primer or probe, such as a primer or probe of DNA, RNA or a nucleic acid analogue such as peptide nucleic acid (PNA) or locked nucleic acid (LNA).

12. The method according to claim 11, wherein the nucleotide primer or probe is capable of hybridising to a subsequence of the region corresponding to SEQ ID NO: 1, or a part thereof, or a region complementary to SEQ ID NO:1.

13. The method according to claim 11, wherein the primer or probe has a length of at least 9 nucleotide or peptide monomers.

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14. The method according to any of the preceding claims 11-13, wherein at least
   one primer or probe is capable of hybridising to a subsequence selected from
   the group of subsequences

5   1. GCTCTGAAAC TTACTAGCCC(A/G)GTATTTATGG AGAGGCATTT

     2. GTGGTCAAAT TCTCATTCAT CGTGG (T/C) CCAGGCAAGC
         ACACTTCCTC

     3. ACCCTGAGGT GAGCACCTGT TCCTT(C/T) TCCTTGCCCT TAGCCCA-
         GAG GTAGA

10   4. GGGCAGGGGT TTGTGCCTCC AATGA (G/A) CACAAGCTCC
         CCCTGCCCCC CAACT

     5. CCTGGCGGTG GCCGTCACCA GCTTT (T/C) GGGGGTGTTT
         GGGAAGCTGG

     6. CTCCAGCCCC ACTGTTCCCT (A/G) GGCCCTATTG GTCCCCCTGG

15   7. ACAAGGAGGA GGCAGAAGTG AGGTT (G/C) AAACCCACTG CCCAATC-
         TTA

     8. CCAACACGGT GAAACCCCGT CTGTA(T/C)TAAAAATACA AAAATTAGCC

     9. AATCCAGGAC CCCATAATCT TCCGT (C/T) ATCTAAAACA ATA-
         ATGGTGA

20   10. CCCAAGGGGG CGAGGGGAGG GTGAA (A/G)GGGTGGGACG
         GGGGCAGCCG

     11. GAAGTGAGAA GGGGGCTGGG GGTCG (G/-) CGCTCGCTAG
         CGGGCGCGGG

     12. CGCACGCGCA GTATCCCGAT TGGCT (C/G)TGCCCTAGCG GATT-
25   GACGGG

     13. AACTCCTGGG TTCGATCAAT ACTCA (GACA/-) ATCTTGGCAG
         GCGCAGGAGG

     14. GCTGGGATTA CAGGCTTGAG CCACC (A/G) CGCCCGGCCT
         GCAAAGCCAT

30   15. TTTTGTATCT TTAGTAGAGA CAGG (T/G) TTTCTCCATG TTGGTCAGGC

     16. GCCTCAGCCT CCCGAGTAGC TGAGACT (C/A) CAGGTGCCCG CCAC-
         CACGCC

     17. TGAAATTGTA GGTTGAGAGG CCAGGCG (C/T) GGTGCTCACG
         CCTGTAATTT

35   18. GTTTATAAAC ATTAAACCAG (T/A) GCTGTGTGAA GGCACTTAAT

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19. CCGTCTCTAT TAAAAATATA AAA (A/C) AATTTAGCCG GGTGTAGCGG

20. GGGAGGCTCG AGGCGGGC (A/G) GATTGCATGA GCTCAGGATT

21. TCCCAAGTTT CAGGGCCCAA (T/G) ATTCTCAAAT CACAGGATTC

22. TGCAGTGAGC TGAGATCGC (A/G) CCACTGCACT CCAGCCTGGG

5   23. TCTTAGGACG CATGGGGGT (T/G) GAGAGAACGG GGAGATAGAC

24. CTGGGTTCTA GAACTACC (C/T) ATGCAAACCC AGCTGTTTCC

25. ATTCTGCCCT GGGTTCTAGA ACTACCT (C/A) TGCAAACCCA
    GCTGTTTCCC

26. GCTGTTTCCC ACCCCATAAG GCA (A/G) TAGGGGAGCC
10   CACCTCCGCC

27. GACCTAGAAG ATCGGTCGAG A (C/T) AGCAGCTTGA GGCTGGCAGG

28. CTGGCCAGGA ATGCAGTCGG GTCAC (C/T) CTGTCTAGCC
    ACCGTCTCGC

29. GGGAGGAGTC GCCGATCAGG (C/T) CCCTTCCTGA AAGTCATCGA

15   30. GCAGCCCGGG CTACAGGGTT (A/G) CCTGAGGTGT GGGTCCCAGG

31. TAGAAATACT AACAAAGGGC (T/C) GTGGGTTTCT CCCCCTGCTT

32. ACAGGAGAGG GAAGGTTTTTTG (A/T) TTTTTTTTTT GTTTTTTTTT

33. GAAGAGGAAG AAGCCCAAAG GGA (A/C) AGAAACCTTC GAGCCA-
    GAAG

20   34. GCGCCTCAAC AGCCAGAAGG AGCG (A/G) AGCCTCAGGC CCAGG-
    CAGCT

35. TTGAGACTCT CTGTTTGAT (A/G) CTTCACTCAG AAGGTGCTTC

36. AGGCCAGGCT CCTGCTGGCT G (C/G) GCTGGTGCAG TCTCTGGGGA

37. CCCCTATACC CTCAAGCAT (C/T) TATCCATTGA GTTACAAACA

25   38. ACCATCCCCC GCCTTCCGTT (A/C) GTCCGGCCCC CGAGGCTAGC

or to a sequence complementary to any of the subsequences.

15. The method according to claim 14, wherein at least one nucleotide probe is se-
30   lected from the group consisting of

1. TGAAATTGTA GGTTGAGAGG CCAGGCG (C/T) GGTGCTCACG
    CCTGTAATTT

2. GTTTATAAAC ATTAAACCAG (T/A) GCTGTGTGAA GGCACTTAAT

35   3. CCGTCTCTAT TAAAAATATA AAA (A/C) AATTTAGCCG GGTGTAGCGG

5

    4. GGGAGGCTCG AGGCGGGC (A/G) GATTGCATGA GCTCAGGATT

    5. TCCCAAGTTT CAGGGCCCAA (T/G) ATTCTCAAAT CACAGGATTC

    6. TGCAGTGAGC TGAGATCGC (A/G) CCACTGCACT CCAGCCTGGG

    7. TCTTAGGACG CATGGGGGT (T/G) GAGAGAACGG GGAGATAGAC

    8. CTGGGTTCTA GAACTACC (C/T) ATGCAAACCC AGCTGTTTCC

    9. ATTCTGCCCT GGGTTCTAGA ACTACCT (C/A) TGCAAACCCA
        GCTGTTTCCC

    10. GCTGTTTCCC ACCCCATAAG GCA (A/G) TAGGGGAGCC
        CACCTCCGCC

    11. GACCTAGAAG ATCGGTCGAG A (C/T) AGCAGCTTGA GGCTGGCAGG

    12. CTGGCCAGGA ATGCAGTCGG GTCAC (C/T) CTGTCTAGCC
        ACCGTCTCGC

    13. GGGAGGAGTC GCCGATCAGG (C/T) CCCTTCCTGA AAGTCATCGA

    14. GCAGCCCGGG CTACAGGGTT (A/G) CCTGAGGTGT GGGTCCCAGG

    15. TAGAAATACT AACAAAGGGC (T/C) GTGGGTTTCT CCCCCTGCTT

    16. ACAGGAGAGG GAAGGTTTTTTG (A/T) TTTTTTTTTT GTTTTTTTTT

    17. GAAGAGGAAG AAGCCCAAAG GGA (A/C) AGAAACCTTC GAGCCA-
        GAAG

    18. GCGCCTCAAC AGCCAGAAGG AGCG (A/G) AGCCTCAGGC CCAGG-
        CAGCT

    or to a sequence complementary to any of the subsequences.

16. The method according to claim 15, wherein at least one nucleotide probe is se-
lected from the group consisting of

    1. GTTTATAAAC ATTAAACCAG (T/A) GCTGTGTGAA GGCACTTAAT

    2. CCGTCTCTAT TAAAAATATA AAA (A/C) AATTTAGCCG GGTGTAGCGG

    3. GGGAGGCTCG AGGCGGGC (A/G) GATTGCATGA GCTCAGGATT

    4. TCCCAAGTTT CAGGGCCCAA (T/G) ATTCTCAAAT CACAGGATTC

    5. TGCAGTGAGC TGAGATCGC (A/G) CCACTGCACT CCAGCCTGGG

    or to a sequence complementary to any of the subsequences.

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17. The method according to any of the preceding claims, wherein at least one se-
quence polymorphism is assessed in a region corresponding to SEQ ID NO: 1
position 1521-37752 (r).

5   18. The method according to any of the preceding claims, wherein at least one se-
quence polymorphism is assessed in a region corresponding to SEQ ID NO: 1
position 7760-22885 (RAI).

19. The method according to any of the preceding claims, wherein at least one se-
10   quence polymorphism is assessed in a region corresponding to SEQ ID NO: 1
position 34391- 37752.

20. The method according to any of the preceding claims, wherein at least two diffe-
rent probes are used, one probe being selected from the probes as defined in
15   any of claims 13-16, and the other probe being capable of hybridising to a se-
quence different from SEQ ID NO: 1, or a part thereof, or to a sequence com-
plementary to a region different from SEQ ID NO: 1, or a part thereof,.

21. The method according to claim 1, wherein the translational product from a se-
20   quence in a region corresponding to SEQ ID NO: 1, or a part thereof, is an anti-
body, such as a monoclonal or polyclonal antibody.

22. A method for estimating the disease prognosis of an individual comprising

25

- assessing in the genetic material of a sample from said individual a sequence
polymorphism

- in a region corresponding to SEQ ID NO: 2, or a part thereof, or
30   - in a region complementary to SEQ ID NO: 2, or a part thereof, or
- in a transcription product from a sequence in a region corresponding to
SEQ ID NO: 2, or a part thereof, or
- or translation product from a sequence in a region corresponding to SEQ ID
NO: 2, or a part thereof,
35   - obtaining a sequence polymorphism response,

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- estimating the disease prognosis of said individual based on the sequence polymorphism response.

23. The method according to claim 22, wherein the method has any of the features as defined in any of the claims 2-21.

24. A method for estimating a treatment response of an individual suffering from cancer to a disease treatment, comprising

- assessing in the genetic material of a sample from said individual a sequence polymorphism

- in a region corresponding to SEQ ID NO: 1, or a part thereof, or
- in a region complementary to SEQ ID NO: 1, or a part thereof, or
- in a transcription product from a sequence in a region corresponding to SEQ ID NO: 1, or a part thereof, or
- or translation product from a sequence in a region corresponding to SEQ ID NO: 1, or a part thereof,
- obtaining a sequence polymorphism response,

- estimating the individual's response to the disease treatment based on the sequence polymorphism response.

25. The method according to claim 24, wherein the method has any of the features as defined in any of the claims 2-21.

26. A primer or probe for detecting polymorphisms for use in a method as defined in any of the claims above, said primer or probe being selected from

TGGCTAACACGGTGAAACC(SEQ ID NO:7)
GGAATCCAAAGATTCTATGATGG(SEQ ID NO:8)
GGGAGGCGGAGCTTGCAGTGA (SEQ ID NO:9)
CTGAGATCGCACCACTGCAC (SEQ ID NO:10)
GGTTTTCTGCTCTGCACACG (SEQ ID NO:11)

8

CCTTTCTCCTTCCACCAACG (SEQ ID NO:12)

CGGGCTACAGGGTTACCTGAG (SEQ ID NO:13)

TCTGCAACCTGGTGCGAGCAGC (SEQ ID NO:14)

CCTACCACCATCATCACATCC (SEQ ID NO:15)

GCCTTGCCAAAAATCATAACC (SEQ ID NO:16)

CCTCTCCCCAATTAAGTGCCTTCACACAGC (SEQ ID NO:17)

AGCCAGGGAGGTTGAGGCT (SEQ ID NO:18)

AGACAGCCCTGAATCAGCAC (SEQ ID NO:19)

GCAATGAGCCGAGATAGAA (SEQ ID NO:20)

TGGCTAGCCCATTACTCTA (SEQ ID NO:21)

27. The primer or probe according to claim 26, wherein the probe is operably linked to at least one label, such as operably linked to two different labels.

28. The probe according to claim 27, wherein the label is selected from TEX, TET, TAM, ROX, R6G, ORG, HEX, FLU, FAM, DABSYL, Cy7, Cy5, Cy3, BOFL, BOF, BO-X, BO-TRX, BO-TMR, JOE, 6JOE, VIC, 6FAM, LCRed640, LCRed705, TAMRA, Biotin, Digoxigenin, DuO-family, Daq-family.

29. The primer or probe according to any of claims 26-28, wherein the primer or probe is operably linked to a surface.

30. The primer or probe according to claim 29, wherein the surface is the surface of microbeads or a DNA chip.

31. A kit for use in a method as defined in any of the claims above, comprising at least one primer or probe, said probe being as defined in any of claims 26-30, and optionally further amplifying means for nucleic acid amplification.